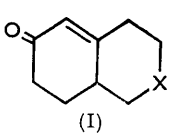
400. *Decahydroisoquinolines and Related Compounds. Part II.* Some Further Examples of Abnormal Ultraviolet Absorption.*

By C. B. Clarke and A. R. Pinder.

Ultraviolet-absorption studies on a series of basic αβ-unsaturated ketones have shown that the compounds absorb at abnormally short wavelengths. The effect is enhanced by quaternisation of the basic groups. Possible explanations of the behaviour are discussed.

Attention has been drawn [1,2] to the fact that the basic αβ-unsaturated ketone 1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-octahydro-2-methyl-6-oxo*iso*quinoline (I; X = NMe) absorbs maximally in the ultraviolet region at an abnormally short wavelength. Similar behaviour has been reported [2] for a 1-aryl derivative of compound (I; X = NH) and very recently [3] for the thio*iso*chroman (I; X = S).

It seemed from these observations that this behaviour might be general for αβ-unsaturated ketones containing basic and possibly other electron-donating groups, not directly united with the chromophore, but separated from it by a saturated carbon chain. We have now prepared a series of basic αβ-unsaturated ketones, and find that such compounds do absorb maximally at unexpectedly short wavelengths, the magnitude of the hypsochromic effect depending on the length of the intervening carbon chain. The effect is also observed with an *N*-acetylated ketonic base, and is enhanced by quaternisation of the nitrogen atom or conversion into the amine oxide. The compounds studied, which may be formulated by the general expression $>N\cdot[C]_n\cdot C=C-C=O$, and the absorptions, are summarised in the Table. Comparison has been made in each case with the value of $\lambda_{max.}$



(I)

* Part I, *J.*, 1956, 327.

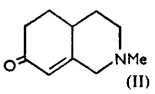
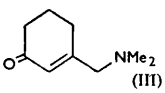
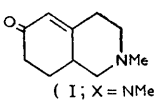
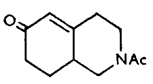
[1] Marchant and Pinder, *Chem. and Ind.*, 1953, 1366; 1954, 1261; *J.*, 1956, 327.
[2] Georgian, *Chem. and Ind.*, 1954, 930.
[3] *Idem, ibid.*, 1957, 1480.

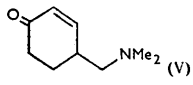
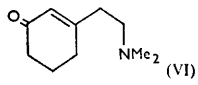
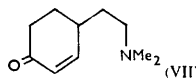
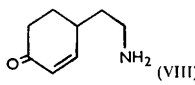
calculated by use of Woodward's rules for the prediction of the position of maximum absorption,[4] or with the observed value for a model αβ-unsaturated ketone (cf. Table).

The cyclic ketones were prepared by reduction, with sodium and liquid ammonia, of a series of aminoalkyl derivatives of anisole, followed by acid hydrolysis.[5] The reduction of 1 : 2 : 3 : 4-tetrahydro-7-methoxy-2-methyl*iso*quinoline afforded the hexahydro-derivative (XII), which was crystalline and on hydrolysis yielded mainly the reduced *iso*quinolone (II), though infrared measurements indicated the presence of a small quantity of the unconjugated ketone (XIII) even after prolonged acid hydrolysis. Catalytic hydrogenation of the ketone (II) gave the corresponding decahydro-oxo*iso*quinoline (XIV), which showed normal infrared carbonyl absorption, indicating that there is no transannular amide-type interaction between the carbonyl group and the nitrogen atom.[6] Similar normal behaviour is shown by the reduction products of several of the ketones studied.

3-Dimethylamino-2 : 2-dimethylpropionaldehyde (XV) was obtained from *iso*butyraldehyde by a Mannich reaction. Condensation with acetone then afforded 6-dimethylamino-5 : 5-dimethylhex-3-en-2-one (IX).

Ultraviolet absorption (mμ) *of basic αβ-unsaturated ketones and related compounds in methanol.*

Ketone	$\lambda_{max.}$ obs.†	$\lambda_{max.}$ calc.	$-\Delta\lambda$
 (II)	222	244	22
Methiodide	218	244	26
 (III)	225	239	14
Methiodide	222	239	17
 (I; X = NMe)	227·5	244	16·5
Methiodide [1-3]	222	244	22
 (IV)	234	244	10
$Me_2C{\cdot}CH{=}CH{\cdot}COMe$ $CH_2{\cdot}NMe_2$ (IX)	222	227	5
Methiodide	220	227	7

Ketone	$\lambda_{max.}$ obs.†	$\lambda_{max.}$ calc.	$-\Delta\lambda$
 (V)	225	227	2
Methiodide	220	227	7
 (VI)	228·5	239	10·5
Methiodide	221	239	18
N-Oxide	220	239	19
 (VII)	224	227	3
Methiodide	220	227	7
 (VIII)	224	227	3
$Et_2N{\cdot}CH_2{\cdot}CH{=}CH{\cdot}COMe$ (X)	218	224 *	6
$Et_2N{\cdot}CH_2{\cdot}CH{=}CH{\cdot}COPh$ (XI)	248	256 **	8

* Observed value for ethylideneacetone (Evans and Gillam, *J.*, 1941, 815).
** Observed value for crotonophenone (Mariella and Raube, *J. Amer. Chem. Soc.*, 1952, **74**, 521).
† log $\varepsilon_{max.}$ 3·7—4·1 (bases), 4·2—4·4 (methiodides).

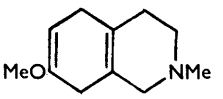
5-Diethylaminopent-3-en-2-ol (XVI; R = Me) was synthesised from but-3-yn-2-ol, which was converted into its acetate and thence *via* a Mannich reaction into 4-acetoxy-1-diethylaminopent-2-yne (XVII). Hydrolysis followed by partial hydrogenation with Lindlar's catalyst afforded the alcohol (XVI; R = Me), which presumably has the *cis*-configuration.[7] Attempts to oxidize this compound to the ketone (X) with chromic acid

[4] Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123; 1942, **64**, 76.
[5] Cf. Birch, *J.*, 1944, 430, and later papers.
[6] Cf. Anet, Bailey, and Robinson, *Chem. and Ind.*, 1953, 944; Leonard and co-workers, *J. Amer. Chem. Soc.*, 1954, **76**, 630, 3463, 5708.
[7] Raphael, "Acetylenic Compounds in Organic Synthesis," Butterworths, London, 1955, pp. 26, 201.

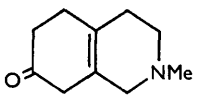
or manganese dioxide gave an impure product containing some (X), as shown by the ultraviolet absorption, but the product showed a strong infrared band in the OH and NH region. This may be explained by incomplete oxidation or, more probably, in view of recent observations of the oxidation of tertiary amines by manganese dioxide,[8] by oxidative attack of the NEt_2 group with formation of the formyl derivative of the corresponding primary amine : $R{\cdot}NEt_2 \xrightarrow{O} R{\cdot}NH{\cdot}CHO + Me{\cdot}CHO$. An analogous series of reactions with 1-phenylprop-1-yn-1-ol resulted in 4-diethylamino-1-phenylbut-2-en-1-ol (XVI; R = Ph); this alcohol behaved similarly on oxidation, yielding a mixture of products containing some of the corresponding ketone (XI).

2-Acetyl-1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-octahydro-6-oxo*iso*quinoline (IV) was obtained from 1 : 2 : 3 : 4-tetrahydro-6-methoxy*iso*quinoline by reduction with sodium and liquid ammonia, followed by acetylation and partial hydrolysis.

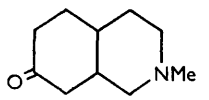
It is apparent from the Table that when the nitrogen atom is separated from the chromophore by a single carbon atom a strong hypsochromic effect is in most cases observed (6—22 mμ). Quaternisation of the nitrogen atom enhances the effect by a further 4—5 mμ. When two carbon atoms separate the groups the shift is smaller (2—10·5 mμ), and is again enhanced by quaternisation or conversion into the amine oxide, but



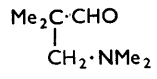
(XII)



(XIII)



(XIV)



(XV)

is reduced by neutralisation of the basic character of the nitrogen atom by acetylation. It is rather surprising that 4-dimethylaminomethyl*cyclo*hex-2-en-1-one (V) shows a very small effect, but this is in harmony with the observation that thebainone-A (XVIII) shows a similarly small shift.[3] When there are more than two carbon atoms between nitrogen atom and chromophore the hypsochromic shift is very small, but even in these cases quaternisation causes a measurable effect.

An explanation of the hypsochromic effect shown by the quaternary salts and the amine oxide [and also by the sulphonium salt (I; X = $^+$SMe) and the sulphone [3] (I; X = SO_2)] does not seem to present any difficulty. Presumably the strong electron-attracting inductive influence of the positive centre is transmitted through the carbon chain to the chromophore, as, for example, in the nitration [9] of quaternary ammonium salts of the type $Ph{\cdot}[CH_2]_n{\cdot}NMe_3^+$ (several other cases of interaction between groups through a saturated carbon chain are known [10]).

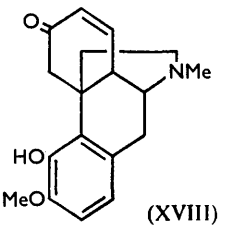
The behaviour of the ketonic bases is not so readily accounted for. Amino-groups of the type $>NR$ and $-NR_2$ (R = H or alkyl) are known to be electron-attracting in an inductive sense,[11] and perhaps the hypsochromic effects could here also be explained in terms of an inductive effect. However, the basic group is not strongly electrophilic, especially compared with a positively charged group, and there is only a small extra hypsochromic effect associated with the establishment of a positive charge on the nitrogen atom. Further, the *N*-acetyl ketone (IV) shows a smaller hypsochromic shift than the base (I; X = NMe), whereas owing to resonance of the type $>\overset{+}{N}{=}C(O^-){-}CH_3$ in the amide it was to be expected that this compound would absorb maximally at no longer a wavelength than does the base (I; X = NMe), if an inductive effect solely is at play.

[8] Henbest and Thomas, *Chem. and Ind.*, 1956, 1097.
[9] Goss, Ingold, and Wilson, *J.*, 1926, 2440; Goss, Hanhart, and Ingold, *J.*, 1927, 250; Ingold and Wilson, *ibid.*, p. 810.
[10] Braude, *J.*, 1949, 1902; Jeffrey, *Proc. Roy. Soc.*, 1947, *A*, **188**, 222; Bateman and Jeffrey, *Nature*, 1943, **152**, 446; Nielsen, *Chem. and Ind.*, 1957, 1358.
[11] Waters, " Physical Aspects of Organic Chemistry," Routledge, 2nd Edition, 1937, p. 209.

In Part I it was postulated that for the free bases the hypsochromic effect was due to the contribution to the stable state of the molecules made by dipolar structures such as (XIX). The reduction in the effect accompanying *N*-acylation may then be attributed to a decrease in the electron-donating capacity of the nitrogen atom as a result of the resonance described. However, the existence of the ketone (XX) in a dipolar form (XXI) has been offered as an explanation of a bathochromic shift, *viz.*, the maximal

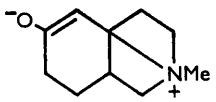
$Et_2N{\cdot}CH_2CH{=}CH{\cdot}CHR{\cdot}OH$ (XVI)

$Et_2N{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CHMe{\cdot}OAc$ (XVII)

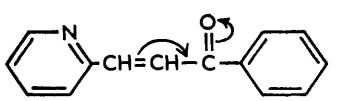


(XVIII)

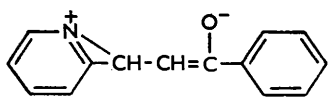
absorption of the ketone at a longer wavelength than that for the corresponding 3- and 4-isomer (all three ketones, however, showing strong hypsochromic shifts relative to benzylideneacetophenone).[12]



(XIX)



(XX)



(XXI)

The ultraviolet absorption of dipolar structures such as (XIX) may be regarded as that of a single ethylenic bond bearing a highly polar oxygen substituent. A model for comparison would be the enolate anion of a monoketone, but the spectra of such structures seem not to have been recorded. There can be little doubt, however, that the substituent will have a strong bathochromic effect, so that maximal absorption will be shifted from the 175 mμ region, characteristic of ethylene, to the 220—240 mμ region (cf. $CHMe{=}CH{\cdot}CO_2H$ and $MeO{\cdot}CMe{=}CH{\cdot}CO_2H$, $\Delta\lambda_{max.}$ +30 mμ; $CH_2{=}CH_2$ and $CH_2{=}CH{\cdot}S{\cdot}CH_2{\cdot}CH_2Cl$, $\Delta\lambda_{max.}$ +53 mμ).[13]

The observed infrared absorption of the bases is normal for αβ-unsaturated ketones. This is difficult to explain on the basis of the dipolar structures. Recent studies on the infrared absorption of enolate anions show that enolisable compounds such as acetylacetone show no carbonyl stretching band in the 1715 $cm.^{-1}$ region, and have strong enolate anion bands in the 1660 $cm.^{-1}$ region.[14] The basic ketones here investigated all show carbonyl bands in the 1665—1685 $cm.^{-1}$ region, and no enolate anion bands.

Experimental

Unless otherwise stated, ultraviolet absorption data refer to solutions in methanol, and infrared data to liquid film or Nujol mulls, and methiodides crystallised from ethanol in needles.

1 : 2 : 3 : 4-*Tetrahydro-7-methoxy-2-methyl*isoquinoline.—Platinum oxide catalyst (0·35 g.), suspended in glacial acetic acid (25 c.c.), was pre-reduced by hydrogen at room temperature and pressure. 7-Methoxy*iso*quinoline [15] (4·0 g.) in acetic acid (50 c.c.) was added and reduction effected for 12 hr. (absorption 2 mols.). The filtered solution was concentrated under reduced pressure from the water-bath, the residual syrup dissolved in a little water, and the solution basified. 1 : 2 : 3 : 4-Tetrahydro-7-methoxy*iso*quinoline, isolated with ether, distilled at 146°/11 mm. (3·5 g.) (hydrochloride, m. p. 228—229°) (lit.: [15] b. p. 184—186°/50 mm.; hydrochloride, m. p. 228—229°). Methylation [16] of the base (6·8 g.) with 90% formic acid (5·8 g.)

[12] Coleman, *J. Org. Chem.*, 1956, **21**, 1193; Marvel and Stille, *ibid.*, 1957, **22**, 1451.
[13] Braude, *Ann. Reports*, 1945, **42**, 119; Bowden, Braude, and Jones, *J.*, 1946, 948.
[14] Bender and Figueras, *J. Amer. Chem. Soc.*, 1953, **75**, 6304.
[15] Fritsch, *Annalen*, 1895, **286**, 1.
[16] Cf. Clarke, Gillespie, and Weisshaus, *J. Amer. Chem. Soc.*, 1933, **55**, 4571.

and 35% aqueous formaldehyde (2·5 g.) for 8 hr. at 95—100° gave, after basification and ether-extraction, 1 : 2 : 3 : 4-tetrahydro-7-methoxy-2-methyl*iso*quinoline (5·6 g.), b. p. 131—135°/10 mm. (hydrochloride, m. p. 205°) (lit.: [15] b. p. 179°/50 mm.; hydrochloride, m. p. 201—202°).

1 : 2 : 3 : 4 : 5 : 8-*Hexahydro*-7-*methoxy*-2-*methyl*isoquinoline (XII).—The following conditions are typical of the sodium–liquid ammonia reductions described in this paper. The foregoing tertiary base (3·75 g.) in methanol (15 c.c.) was added gradually, with stirring, to liquid ammonia (300 c.c.) containing dry ether (20 c.c.), followed by sodium (3·0 g.) in small pieces during 1 hr. When all the sodium had dissolved, ether (100 c.c.) was added, followed by water (100 c.c.), and after being kept overnight the solution was thoroughly extracted with ether, and the combined extracts were dried and evaporated. The residual 1 : 2 : 3 : 4 : 5 : 8-*hexahydro*-7-*methoxy*-2-*methyl*isoquinoline distilled at 126°/8 mm., 140°/10 mm. (3·4 g.), solidified, and separated from light petroleum (b. p. 40—60°) in needles, m. p. 50—51° (Found: C, 73·7; H, 9·3. $C_{11}H_{17}ON$ requires C, 73·7; H, 9·5%). The *methiodide*, formed readily by mixing the base with methyl iodide, had m. p. 222° (Found: C, 44·8; H, 6·3. $C_{12}H_{20}ONI$ requires C, 44·9; H, 6·2%).

1 : 2 : 3 : 4 : 5 : 6 : 7 : 10-*Octahydro*-2-*methyl*-7-*oxo*isoquinoline (II).—The above hexahydro-base (2·0 g.) was boiled under reflux for 5 hr. with 2N-sulphuric acid (75 c.c.). The cooled solution was basified and the product isolated with ether. 1 : 2 : 3 : 4 : 5 : 6 : 7 : 10-*Octahydro*-2-*methyl*-7-*oxo*isoquinoline distilled at 58—60°/0·05 mm. (1·3 g.) (Found: C, 72·4; H, 9·0. $C_{10}H_{15}ON$ requires C, 72·7; H, 9·1%), $\lambda_{max.}$ 222 mμ (ε 5100), infrared carbonyl bands at 1665 (strong) and 1710 cm.$^{-1}$ (weak). The *methiodide* formed pale cream prisms, m. p. 205—208° (Found: C, 43·0; H, 5·7. $C_{11}H_{18}ONI$ requires C, 43·0; H, 5·9%), $\lambda_{max.}$ 218 mμ (ε 22,400).

Decahydro-2-*methyl*-7-*oxo*isoquinoline (XIV).—The preceding keto-base (1·0 g.) in acetic acid (20 c.c.) was shaken with Adams platinum oxide in hydrogen at room temperature and pressure for 3 hr. (uptake 1 mol.). The solution was filtered and evaporated and the residue taken up in a little water. *Decahydro*-2-*methyl*-7-*oxo*isoquinoline, isolated by basification and ether-extraction, distilled at 61—63°/0·03 mm. (0·85 g.) (Found: C, 71·8; H, 9·9. $C_{10}H_{17}ON$ requires C, 71·9; H, 10·2%). Infrared absorption: strong carbonyl band at 1703 cm.$^{-1}$. The *methiodide* had m. p. 258—259° (Found: C, 42·7; H, 6·8. $C_{11}H_{20}ONI$ requires C, 42·7; H, 6·5%).

3-*Dimethylaminomethyl*cyclo*hex*-2-*enone* (III).—3-Methoxybenzylamine (10·0 g.), obtained by the reduction of *m*-anisaldoxime,[17] was methylated with 90% formic acid (16·8 g.) and 40% formaldehyde (6·5 g.) during 7 hr. at 95—100°. Basification of the cooled solution, followed by ether-extraction, afforded 3-methoxy-*NN*-dimethylbenzylamine, b. p. 106°/10 mm. (4·6 g.) (lit.,[18] b. p. 105°/13 mm.) [*methiodide*, m. p. 142—143° (Found: C, 42·6; H, 6·0. $C_{11}H_{18}ONI$ requires C, 43·0; H, 5·9%)]. Reduction of the tertiary base (4·0 g.) with sodium (3·9 g.) in liquid ammonia (300 c.c.) containing methanol (20 c.c.) gave 3-*dimethylaminomethyl*-2 : 5-*dihydroanisole*, b. p. 93—96°/8 mm. (3·2 g.) (Found: C, 71·7; H, 10·1. $C_{10}H_{17}ON$ requires C, 71·9; H, 10·2%) [*methiodide*, m. p. 145° (Found: C, 42·7; H, 6·2. $C_{11}H_{20}ONI$ requires C, 42·7; H, 6·5%)]. Hydrolysis of the dihydro-base (2·0 g.) by boiling 2N-sulphuric acid (75 c.c.) for 1 hr. gave 3-*dimethylaminomethyl*cyclo*hex*-2-*enone*, b. p. 116—118°/22 mm. (1·2 g.) (Found: C, 70·8; H, 9·7. $C_9H_{15}ON$ requires C, 70·6; H, 9·8%), $\lambda_{max.}$ 225 mμ (ε 5950) [*methiodide*, m. p. 170—171° (Found: C, 40·8; H, 6·3. $C_{10}H_{18}ONI$ requires C, 40·7; H, 6·1%), $\lambda_{max.}$ 222 mμ (ε 23,600)].

4-*Dimethylaminomethyl*cyclo*hex*-2-*enone* (V).—Methylation of 4-methoxybenzylamine [19] (9·0 g.) with 90% formic acid (10·0 g.) and 40% formaldehyde (13·0 g.) for 3 hr. gave *NN*-dimethylanisylamine, b. p. 106—108°/11 mm. (8·5 g.) (lit.,[18] b. p. 109°/13 mm.). Reduction of the tertiary base (8·5 g.) with sodium (7·4 g.) in liquid ammonia (300 c.c.) and methanol (25 c.c.) afforded 4-*dimethylaminomethyl*-2 : 5-*dihydroanisole*, b. p. 100—102°/11 mm. (7·2 g.) (Found: C, 71·5; H, 9·9. $C_{10}H_{17}ON$ requires C, 71·9; H, 10·2%) [*methiodide*, in plates, m. p. 233—234° (decomp.) (Found: C, 42·8; H, 6·6. $C_{11}H_{20}ONI$ requires C, 42·7; H, 6·5%)]. Hydrolysis of the dihydro-base (2·0 g.) with 2N-hydrochloric acid (75 c.c.) refluxing under nitrogen for 1 hr. gave two products separated by fractional distillation. The first fraction, b. p. 60—64°/9 mm. (0·5 g.), was nitrogen-free and neutral, gave a positive reaction towards Brady's reagent, and quickly polymerised to a gelatinous material; it was probably 4-methylene*cyclo*hex-2-enone.

[17] Shoppee, *J.*, 1932, 696.
[18] Stedman, *J.*, 1927, 1904.
[19] Jones and Pyman, *J.*, 1925, **127**, 2592, 2596.

The main fraction, b. p. 104—105°/9 mm. (1·4 g.) (Found: C, 71·1; H, 10·2. $C_9H_{15}ON$ requires C, 70·6; H, 9·8%), was 4-*dimethylaminomethyl*cyclo*hex*-2-*enone*, $\lambda_{max.}$ 225 mμ (ε 6140). The 2 : 4-*dinitrophenylhydrazone*, prepared in alcoholic sulphuric acid with subsequent basification with potassium hydrogen carbonate, separated from ethanol in deep red needles, m. p. 131—133° (Found: C, 54·7; H, 5·7. $C_{15}H_{19}O_4N_5$ requires C, 54·1; H, 5·7%) [*methiodide*, m. p. 171—171·5° (Found: C, 40·8; H, 5·7. $C_{10}H_{18}ONI$ requires C, 40·7; H, 6·1%), $\lambda_{max.}$ at 220 mμ (ε 25,000)].

3-2′-*Dimethylaminoethyl*cyclo*hex*-2-*enone* (VI).—3-Methoxy-*NN*-dimethylphenethylamine [20] (4·0 g.), when reduced with sodium (3·1 g.) in liquid ammonia (300 c.c.) containing dry ether (25 c.c.) and methanol (25 c.c.), gave 3-2′-*dimethylaminoethyl*-2 : 5-*dihydroanisole*, b. p. 126°/14 mm. (3·2 g.) (Found: C, 72·8; H, 10·3. $C_{11}H_{19}ON$ requires C, 72·9; H, 10·5%) [*methiodide*, m. p. 139·5—140·5° (Found: C, 44·3; H, 6·7. $C_{12}H_{22}ONI$ requires C, 44·6; H, 6·8%]. Hydrolysis of the reduced base (1·0 g.) by boiling 2N-sulphuric acid (40 c.c) for 1 hr. afforded 3-2′-*dimethylaminoethyl*cyclo*hex*-2-*enone*, b. p. 140°/19 mm. (0·75 g.) (Found: C, 72·4; H, 10·0. $C_{10}H_{17}ON$ requires C, 71·9; H, 10·2%), $\lambda_{max.}$ 228·5 mμ (ε 8500) [*methiodide*, plates, m. p. 176—177° (Found: C, 42·9; H, 6·2. $C_{11}H_{20}ONI$ requires C, 42·7; H, 6·5%), $\lambda_{max.}$ 221 mμ (ε 16,000)]. The N-*oxide* was obtained by mixing the base (0·74 g.) in ethanol (10 c.c.) with 30% hydrogen peroxide (0·7 c.c.). After 2 days at room temperature the solution was treated with charcoal, filtered, and evaporated, leaving the oxide as a neutral thick syrup (0·7 g.), $\lambda_{max.}$ 220 mμ (ε 8000). Passage of sulphur dioxide for several hours through an aqueous solution of the product regenerated, on basification, the original base (methiodide, m. p. and mixed m. p. 176—177°). Hydrogenation of the unsaturated ketonic base (0·5 g.) in ethanol (15 c.c.) with 5% palladised charcoal (200 mg.) for 2 hr. at room temperature and pressure (uptake 1 mol.) afforded 3-2′-*dimethylaminoethyl*cyclo*hexanone*, b. p. 134—136°/19 mm. (0·5 g.) (Found: C, 70·8; H, 11·4. $C_{10}H_{19}ON$ requires C, 71·0; H, 11·2%). Infrared absorption : strong carbonyl bands at 1700 cm.$^{-1}$ (liquid film) and 1718 cm.$^{-1}$ (in CCl_4).

The *methiodide* had m. p. 185° (decomp.) (Found: C, 42·2; H, 7·0. $C_{11}H_{22}ONI$ requires C, 42·4; H, 7·1%) and a strong infrared carbonyl band at 1705 cm.$^{-1}$ (in Nujol).

4-2′-*Dimethylaminoethyl*cyclo*hex*-2-*enone* (VII).—Reduction of *p*-methoxy-ω-nitrostyrene [21] (4·0 g.) in dry ether (100 c.c.) with lithium aluminium hydride (3·0 g.) suspended in dry ether (150 c.c.), under the usual conditions,[22] gave 4-methoxyphenethylamine, b. p. 126—128°/10 mm. (2·6 g.) (lit.,[23] b. p. 136°/16 mm.). Methylation [20] of the base with 98% formic acid (14·7 g.) and 40% formaldehyde (12·1 g.) afforded *O*-methylhordenine, b. p. 84°/0·5 mm., 108°/11 mm. (8·2 g.) (lit.,[24] b. p. 253—254°). Reduction of *O*-methylhordenine (8·15 g.) in methanol (30 c.c.) with sodium (6·5 g.) in liquid ammonia (350 c.c.) furnished 2 : 5-*dihydro*-O-*methylhordenine*, b. p. 124°/11 mm. (6·2 g.) (Found: C, 72·7; H, 10·5. $C_{11}H_{19}ON$ requires C, 72·9; H, 10·5%). Hydrolysis of the dihydro-base (1·7 g.) with boiling 2N-sulphuric acid (75 c.c.) for 1 hr. gave, after basification, 4-2′-*dimethylaminoethyl*cyclo*hex*-2-*enone*, b. p. 122°/11 mm. (1·2 g.) (Found: C, 71·6; H, 10·5. $C_{10}H_{17}ON$ requires C, 71·9; H, 10·2%), $\lambda_{max.}$ 224 mμ (ε 4150). Infrared absorption: strong carbonyl band at 1670 cm.$^{-1}$, weak band (unconjugated carbonyl group ?) at 1710 cm.$^{-1}$. The *methiodide* had m. p. 191° (Found: C, 42·1; H, 6·6. $C_{11}H_{20}ONI$ requires C, 42·7; H, 6·5%), $\lambda_{max.}$ 220 mμ (ε 15,500).

A similar reduction of 4-methoxyphenethylamine (5·0 g.) in methanol (25 c.c.) with sodium (4·0 g.) in liquid ammonia (300 c.c.) gave 2 : 5-*dihydro*-4-*methoxyphenethylamine*, b. p. 140°/16 mm. (3·6 g.) (Found: N, 9·1. $C_9H_{15}ON$ requires N, 9·15%), which with boiling 2N-sulphuric acid (100 c.c.) under nitrogen afforded, in 1 hr., 4-2′-*aminoethyl*cyclo*hex*-2-*enone* (VIII), b. p. 124°/11 mm. (2·7 g.) (Found: C, 69·0; H, 9·5. $C_8H_{13}ON$ requires C, 69·1; H, 9·4%), $\lambda_{max.}$ at 224 mμ (ε 6000). The *picrolonate* separated from methanol in yellowish-brown needles, m. p. 185—186° (Found: C, 53·7; H, 5·2. $C_{18}H_{21}O_6N_5$ requires C, 53·6; H, 5·2%).

3-*Dimethylamino*-2 : 2-*dimethylpropionaldehyde* (XV).[25]—*iso*Butyraldehyde (50 g.) and 25% aqueous dimethylamine (100 g.) were mixed and stirred at 25—30° during addition of 40%

[20] Haworth, Lamberton, and Woodcock, *J.*, 1947, 182; Davies, Haworth, Jones, and Lamberton, *ibid.*, p. 191.
[21] Rosemund, *Ber.*, 1909, **42**, 4780; see also Gairaud and Lappin, *J. Org. Chem.*, 1953, **18**, 1.
[22] Compare Hamlin and Weston, *J. Amer. Chem. Soc.*, 1949, **71**, 2210; Erne and Ramirez, *Helv. Chim. Acta*, 1950, **33**, 912.
[23] Schales, *Ber.*, 1935, **68***B*, 1943.
[24] Kindler and Hesse, *Arch. Pharm.*, 1927, **265**, 389.
[25] Cf. Mannich, Lesser, and Silten, *Ber.*, 1932, **65**, 378; see also " Organic Reactions," Vol. I, p. 330.

aqueous formaldehyde (150 g.) over 1 hr. After a further hour at room temperature, then 2 hr. on the water-bath, the mixture was cooled, treated with sodium chloride (150 g.) and potassium carbonate (100 g.), and extracted with ether. The dried extract was concentrated and the residue distilled *in vacuo* through a short Vigreux column. The main fraction was 3-dimethylamino-2 : 2-dimethylpropionaldehyde, b. p. 110—116°/100 mm. (39·7 g.) (lit.,[25] b. p. 142—144°/760 mm.).

6-*Dimethylamino*-5 : 5-*dimethylhex*-3-*en*-2-*one* (IX).—To a solution from sodium (2·5 g.) in absolute ethanol (40 c.c.) cooled to 0° was added the above Mannich base (12·9 g.) mixed with dry acetone (5·8 g.).[26] After the whole had been kept overnight at room temperature water was added, followed by potassium carbonate. 6-*Dimethylamino*-5 : 5-*dimethylhex*-3-*en*-2-*one*, isolated with ether, distilled at 102—104°/10 mm. (4·0 g.) (Found: C, 70·4; H, 11·0. $C_{10}H_{19}ON$ requires C, 71·0; H, 11·2%), and had $\lambda_{max.}$ 222 mμ (ε 13,400) [*methiodide*, m. p. 166—167° (Found: C, 42·7; H, 6·7. $C_{11}H_{22}ONI$ requires C, 42·4; H, 7·1%), $\lambda_{max.}$ 220 mμ (ε 25,950)].

2-*Acetyl*-1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-*octahydro*-6-*oxoisoquinoline* (IV).—Reduction of 1 : 2 : 3 : 4-tetrahydro-6-methoxy*iso*quinoline (3·2 g.) [27] with sodium (3·8 g.) in liquid ammonia (400 c.c.) containing ether (40 c.c.) and methanol (40 c.c.) gave the corresponding hexahydro-base, b. p. 138—140°/14 mm. (3·0 g.). Acetic anhydride (7 c.c.) was added slowly with ice-cooling to this base (2·4 g.), and the mixture kept at room temperature for 10 min. Acetic acid and excess of anhydride were removed *in vacuo* on the water-bath, and the residual 2-*acetyl*-1 : 2 : 3 : 4 : 5 : 8-*hexahydro*-6-*methoxy*isoquinoline distilled (b. p. 132°/0·1 mm.; 2·9 g.). This solidified and separated from methanol in needles, m. p. 70—71° (Found: C, 69·0; H, 8·0. $C_{12}H_{17}O_2N$ requires C, 69·6; H, 8·2%). Hydrolysis of the product by refluxing N-sulphuric acid (40 c.c.) for 30 min., gave, after saturation with ammonium sulphate and ether-extraction, 2-*acetyl*-1 : 2 : 3 : 4 : 6 : 7 : 8 : 9-*octahydro*-6-*oxoisoquinoline*, b. p. 146—148°/0·7 mm. (0·6 g.) (Found: C, 68·3; H, 8·5; *N*-acetyl, 21·4. $C_{11}H_{15}O_2N$ requires C, 68·4; H, 7·8; *N*-acetyl, 22·4%), $\lambda_{max.}$ 234 mμ (ε 7860).

5-*Diethylaminopent*-3-*yn*-2-*ol*.—But-3-yn-2-ol (20·0 g.) and acetic anhydride (40 c.c.) were heated at 105—115° for 3 hr. The excess of anhydride was removed *in vacuo* and the residual 1-methylprop-2-ynyl acetate distilled [b. p. 125—127° (24·5 g.)] (lit.,[28] b. p. 124—126°). The acetate (10·0 g.), dry dioxan (45 c.c.), paraformaldehyde (4·1 g.), and anhydrous diethylamine (8·2 g.) were heated on the water-bath for 24 hr. The solvent was removed *in vacuo*, ether (100 c.c.) added, and the mixture extracted exhaustively with dilute hydrochloric acid. Basification and ether-extraction of the acid solution afforded 4-*acetoxy*-1-*diethylaminopent*-2-*yne* (XVII), b. p. 126°/23 mm. (16·0 g.) (Found: C, 66·9; H, 9·4. $C_{11}H_{19}O_2N$ requires C, 67·0; H, 9·6%). The ester (15·0 g.) in methanol (60 c.c.) was treated with 0·1M-methanolic sodium methoxide (15 c.c.), and the solution kept at room temperature for 12 hr. Evaporation *in vacuo* followed by treatment with water and ether extraction gave 5-*diethylaminopent*-3-*yn*-2-*ol*, b. p. 112—114°/10 mm. (10·5 g.) (Found: C, 69·1; H, 11·0. $C_9H_{17}ON$ requires C, 69·7; H, 11·0%).

5-*Diethylaminopent*-3-*en*-2-*ol* (XVI; R = Me).—The above aminopentenol (5·0 g.) in ethyl acetate (100 c.c.) was shaken in hydrogen at room temperature and pressure with Lindlar's catalyst [29] (0·75 g.). After 30 min. (absorption 1 mol.) the solution was filtered and evaporated under reduced pressure. The residual 5-*diethylaminopent*-3-*en*-2-*ol* distilled at 109—110°/10 mm. (4·4 g.) (Found: C, 68·6; H, 12·3. $C_9H_{19}ON$ requires C, 68·8; H, 12·1%). The *picrolonate*, obtained from benzene solutions, separated from methanol in brownish-yellow prisms, m. p. 138—139° (Found: C, 53·9; H, 6·1. $C_{19}H_{27}O_6N_5$ requires C, 54·2; H, 6·4%).

Oxidation of the above alcohol (2·0 g.) in acetic acid (4 c.c.) with chromium trioxide (0·9 g.) in acetic acid (4 c.c.) and water (2 c.c.) at 55° for 2½ hr., then at room temperature for 12 hr., gave, on basification and ether-extraction, a pale yellow oil, b. p. 104°/18 mm. (0·8 g.) (Found: C, 67·1; H, 12·0. Calc. for $C_9H_{17}ON$: C, 69·7; H, 11·0%). This could not be purified satisfactorily; it showed the properties of an αβ-unsaturated ketone (max. at 218 mμ; ε 2900), but the infrared absorption (liquid film) showed a strong band at 3130 cm.$^{-1}$ (NH group?) in addition to bands at 1679 cm.$^{-1}$ (conjugated carbonyl group) and 1643 cm.$^{-1}$ (C=C). A *picrolonate* separated from methanol in brownish-yellow prisms, m. p. 136° (Found: C, 54·5;

[26] Cf. Eccott and Linstead, *J.*, 1930, 917.
[27] Marchant and Pinder, *J.*, 1956, 327.
[28] Myers, Collett, and Lazzell, *J. Phys. Chem.*, 1952, **56**, 461; Schlichting and Klager, U.S.P. 2,340,701/1944.
[29] Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446.

H, 6·4. $C_{19}H_{25}O_6N_5$ requires C, 54·5; H, 6·0%) which depressed the m. p. of the above picrolonate on admixture. Similar results were obtained when the alcohol was shaken with manganese dioxide [30] under a variety of conditions.

4-Diethylamino-1-phenylbut-2-yn-1-ol.—1-Phenylprop-2-ynyl acetate [31] (15·0 g.), diethylamine (7·85 g.), paraformaldehyde (2·6 g.), and dioxan (40 c.c.) were heated on the water-bath for 24 hr.[32] The solvent was evaporated under reduced pressure, the residue rendered acid with dilute hydrochloric acid, and neutral matter removed with ether. Basification with potassium carbonate and extraction with ether then gave *1-acetoxy-4-diethylamino-1-phenylbut-2-yne*, b. p. 128°/0·25 mm. (16·9 g.) (Found: C, 73·9; H, 8·2. $C_{16}H_{21}O_2N$ requires C, 74·1; H, 8·1%). Hydrolysis of the ester (13·2 g.) in methanol (50 c.c.) with 0·1M-methanolic sodium methoxide (14 c.c.) overnight at room temperature gave, after removal of the solvent and ether-extraction, *4-diethylamino-1-phenylbut-2-yn-1-ol*, which separated from light petroleum (b. p. 40—60°) in needles, m. p. 52—53° (7·8 g.) (Found: C, 76·9; H, 8·5. $C_{14}H_{19}ON$ requires C, 77·4; H, 8·8%).

4-Diethylamino-1-phenylbut-2-en-1-ol (XVI; R = Ph).—The above acetylenic alcohol (2·25 g.) in ethyl acetate (100 c.c.) was shaken in hydrogen at room temperature and pressure with Lindlar's catalyst [29] (0·7 g.) for 15 min. (uptake 1 mol.). The filtered solution was concentrated *in vacuo*; the residual *4-diethylamino-1-phenylbut-2-en-1-ol* distilled at 106—108°/0·15 mm. (1·93 g.) (Found: C, 76·3; H, 9·6. $C_{14}H_{21}ON$ requires C, 76·7; H, 9·6%).

Shaking the reduction product (2·0 g.) in acetone (50 c.c.) with activated manganese dioxide (5·0 g.) [30] at room temperature for 2 hr. under nitrogen gave, after filtration and concentration, a pale yellow oil, b. p. 106—108°/15 mm. (0·43 g.) (Found: C, 76·5; H, 9·5%), which could not be purified satisfactorily but evidently contained some of the desired αβ-unsaturated ketone (XI) (max. at 248 mμ; ε 2030). Infrared absorption (liquid film): bands at 1665 (cross-conjugated carbonyl group) [33] and 3130 cm.$^{-1}$ (NH group ?).

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[30] Cf. Mancera, Rosenkranz, and Sondheimer, *J.*, 1953, 2189.
[31] Cf. Jones and McCombie, *J.*, 1942, 733.
[32] Cf. Jones, Marszak, and Bader, *J.*, 1947, 1578.
[33] Bellamy, " The Infrared Spectra of Complex Molecules," Methuen, London, 1954, p. 114.